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(54) 【発明の名称】 ポリスルホン系多孔質膜

(57) 【要約】

【課題】 製造時に膜同士の間着による成型不良を起こすことなく、しかも、透析液に含まれる菌塊片が膜内部へ侵入しない構造を有するポリスルホン系多孔質膜を提供する。

【解決手段】 ポリスルホン系樹脂と親水性高分子からなり、内面側に緻密層、外表面に開孔部を持った中空糸膜において、特定の孔面積の孔の存在率、平均孔面積、および開孔率を規定すると、汚染透析液に由来する菌塊片の膜内部への侵入を防ぐことができ、かつ、中空糸同士の間着も防止できる。

【効果】 本発明のポリスルホン系多孔質膜は、製造時に膜間着による成型不良を起こすことなく、しかも、透析液に含まれる菌塊片の膜内部へ侵入によるエンドトキシンの逆濾過が事実上起こらないため、血液浄化分野で好適に使用できる。

【特許請求の範囲】

【請求項1】 ポリスルホン系樹脂と親水性高分子からなり、内表面側に緻密層、外表面に開孔部を有する中空糸膜であって、外表面における開孔部の開孔率が10～30%、外表面における孔面積が $0.5\mu\text{m}^2$ 以上の孔の存在率が10%以下、かつ、孔面積が $0.1\mu\text{m}^2$ 以下の孔の存在率が75%以下であること、および/または外表面における平均孔面積が $0.05\sim 0.35\mu\text{m}^2$ であることを特徴とするポリスルホン系多孔質膜。

【請求項2】 親水性高分子がポリビニルピロリドンであることを特徴とする請求項1に記載のポリスルホン系多孔質膜。

【発明の詳細な説明】

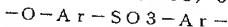
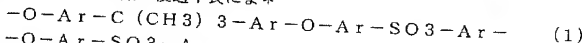
【0001】

【発明の属する技術分野】 本発明は、体外循環による血中老廃物の除去を目的とした医療用分離膜に関するもので、血液浄化、特に腎機能を代用するための血液透析、血液濾過、および血液濾過透析の分野で利用されるものである。

【0002】

【従来の技術】 近年、腎機能の低下により血液中の老廃物除去能力が低い患者に対し、透析膜を用いた透析療法が行われ患者の延命がなされる。一方、このような透析療法の長期化に伴い、透析アミロイドシスと呼ばれる合併症が出現している。これはアミロイドと呼ばれる繊維状蛋白が靱帯、腱、関節などに沈着し、さまざまな臨床症状をもたらす疾患である。このアミロイドを構成する蛋白の一つとして β_2 -ミクログロブリンが同定されて以来、これら低分子蛋白の除去が治療目標の一つとなり、それを可能とする高性能透析膜の市場要求が高まった。高性能透析膜に求められる特性としては、 β_2 -ミクログロブリンに代表される低分子蛋白の高い除去性能、および優れた生体適合性であるが、これらを満足する膜素材として合成高分子であるポリスルホン系樹脂が注目されており、ポリスルホン系樹脂を主体とする高性能透析膜の開発が積極的に進められている。

【0003】 ところが、ポリスルホン系樹脂は疎水性が高く、そのままで水濡れ性が悪いため濾過性能が十分に発揮できない。さらに、本発明のように血液浄化分野で使用される場合、血液凝固系の活性化を抑制する必要もあり、膜表面を親水化するために親水性高分子やグリセリン等の親水化剤が添加される場合が多い。これらの親水化剤は膜表面に存在するため、製造プロセスにおける乾燥時に親水化剤が糊の役目を果たし、隣接する膜同士で固着が生じる結果、ポッティング剤の浸透不良によ*



【0008】 膜を構成する第二の成分は親水性高分子であり、主に膜の親水化と孔形成を目的として添加されている。親水性高分子はポリスルホン系樹脂と共通の溶剤

* なる成型不良が発生することがあった。

【0004】 この欠点を改善する試みは、例えば、中空糸膜の外表面に大きな開孔部を作って隣接する膜同士の接触面積を軽減する技術として、特開平7-289863に開示されている。しかしながら、エンドトキシンカットフィルターの使用によって透析液の水質管理状況が飛躍的に向上した一方で、透析液供給カプラー等の構造因による透析液汚染は依然として発生しており、使用時にカプラーからはがれ落ちた菌塊片が、膜外表面の開孔部から膜内部の多孔質部に侵入していく可能性があった。しかも、これら高性能透析膜においては、侵入時の物理的ショックで菌塊片から遊離したエンドトキシンが緻密層を透過し、血液側に移行して生体を刺激するおそれがあった。

【0005】

【発明が解決しようとする課題】 本発明は、製造時に膜固着による成型不良を起こすことなく、しかも、透析液に含まれる菌塊片が膜内部へ侵入しないポリスルホン系多孔質膜を提供することを目的とする。

【0006】

【課題を解決するための手段】 本発明者らは、上記課題を解決するために鋭意研究した結果、ポリスルホン系樹脂と親水性高分子からなり、内表面側に緻密層、外表面に開孔部を持った中空糸膜において、特定の孔面積の存在率、平均孔面積、および開孔率を特定の範囲にすると、中空糸同士の固着が防止できるのみでなく、汚染透析液から由来する菌塊片の膜内部への侵入を高率に阻止できることを見出し、本発明を完成すに至った。すなわち、本発明は、ポリスルホン系樹脂と親水性高分子からなり、内表面側に緻密層、外表面に開孔部を有する中空糸膜であって、外表面における開孔部の開孔率が10～30%、外表面における孔面積が $0.5\mu\text{m}^2$ 以上の孔の存在率が10%以下、かつ、孔面積が $0.1\mu\text{m}^2$ 以下の孔の存在率が75%以下であること、および/または外表面における平均孔面積が $0.05\sim 0.35\mu\text{m}^2$ であることを特徴とするポリスルホン系多孔質膜に関するものである。

【0007】 本発明の膜は、ポリスルホン系樹脂と親水性高分子からなるが、膜を構成する主な成分はポリスルホン系樹脂であり、下記に示す化学構造式(1)、もしくは(2)のユニットの繰り返し構造からなる。これ以外にも芳香環上に官能基やアルキル基が結合した、いわゆるポリスルホン誘導体も本発明の範疇に含まれる。なお、式中のArはパラ置換の二価フェニル基を示す。

(1)

(2)

に溶解し、相溶性を有するという点からビニル系高分子が好ましく、例えば、ポリビニルピロリドン、ポリエチレングリコール、ポリアミド、ポリビニルアルコール、

エチレンビニルアルコール共重合体から選択することができる。中でも、ポリビニルピロリドンはポリスルホン系樹脂と適度な親和性を有し、膜表面に残って親水化による抗血栓化や濾過性能に寄与できるため、もっとも好ましい。これらの親水性高分子の含有率については、最終的に膜表面を親水化できていればよいので、3~12重量%であれば十分である。より好ましくは5~9重量%である。したがって、膜の残りの部分、88~97重量%がポリスルホン系樹脂である。

【0009】本発明の多孔質膜の構造は、内径が80~400 μm の中空部と厚みが35~85 μm の膜厚部を持つ中空糸状であり、血液浄化用途として十分な耐圧性と引っ張り強度を兼ね備えている。内径がこれ以下に小さいと血流抵抗が高まって血流速度が確保できないが、必要以上に大きくなっても血中の物質移動効率が低下して治療効果の低下につながる。また、膜厚は薄すぎると強度が保てずに潰れやリークの原因となり、厚すぎると膜中の物質移動抵抗が大きくなって透過性能が低下する。この中空糸膜は、内表面側に分離機能を有する緻密層、外表面側に支持体としての粗密層からなる非対称構造をなし、しかも、透析液と接する外表面には制御され*

$$\text{存在率 (\%)} = (\text{任意の孔面積の孔の総数} / \text{画像中の孔の総数}) \times 100 \quad (3)$$

【0012】通常、透析液の一部は膜の外表面の開孔部から膜内部の多孔部に流れ込むが、その透析液にカプラー等由来の菌塊片が含まれると菌塊片が膜内部まで侵入し、侵入時の物理的なショックで菌塊片から遊離したエンドトキシンの一部が、緻密層を通過して血液側に移行して行くことがある。一般に、菌体の大きさは長径が1~3 μm であるため、孔面積が0.5 μm^2 以下では菌塊片の侵入は殆ど起こらない。菌塊片の侵入を事実上阻止するには、孔面積0.5 μm^2 以上の孔の存在率を10%以下に抑えることが必要であり、7%以下に抑えるとともに好ましい。もっとも好ましくは5%以下である。一方、孔面積が小さな孔が増えすぎると今度は成型※

$$\text{平均孔面積} = \text{画像中の孔面積の総和} / \text{画像中の孔総数} \quad (4)$$

平均孔面積も菌塊片の侵入だけではなく、成型性、特に膜同士の固着にも関係している。これは、小さいほど隣接する膜同士が固着する傾向が強くなり、成型不良を生じやすい。反対に大きいほど菌塊片の侵入が起こるため、0.05~0.35 μm^2 の範囲に抑える必要がある。より好ましくは0.10~0.30 μm^2 、もっとも好ましくは0.10~0.20 μm^2 の範囲である。★

$$\text{開孔率 (\%)} = (\text{開孔部の孔面積の総和} / \text{取り込んだ画像の面積}) \times 100 \quad (5)$$

【0015】開孔率は膜同士の固着への寄与に大きく関与し、開孔率が小さいと隣接する膜同士の接触面積が増えて固着が起こり、ひどい場合は、束全体が棒状に固着することさえある。このため、開孔率は10%以上を確保する必要がある。しかし、開孔率を不必要に大きくす

※た孔分布を持った開孔部を有して本発明の効果を発揮している。

【0010】本発明の膜の孔分布は、乾燥膜の外表面の走査型電子顕微鏡写真を画像解析することで数値化される。具体的には膜に付着した孔径保持材や充填液を水洗後、冷エタノールから凍結乾燥した膜を銀蒸着し、電子顕微鏡で倍率6000倍における膜の外表面写真を撮影する。これを90mm×70mmの大きさにプリントし、写真の全範囲を画像解析ソフトを用いてパソコンに取り込み、画像を二値化することで、外表面の各々の開孔部について孔面積を求めることができる。その結果、本発明者らは、孔面積の分布や平均孔面積と透析液中の菌塊片侵入量や成型性との間に一定の関係があること、および開孔率と成型性との間にも一定の関係があつて、いずれをも制御する必要があることを見出した。

【0011】まず第一に、特定の孔面積を有する孔の存在率について説明するが、本発明でいう存在率とは、取り込んだ画像中の孔の総数に対する任意の孔面積の孔の総数の百分率と定義され、下記の式(3)で与えられる。なお、10ピクセル以下はノイズと見なして計数から除外した。

$$\text{存在率 (\%)} = (\text{任意の孔面積の孔の総数} / \text{画像中の孔の総数}) \times 100 \quad (3)$$

※上の問題が起こりやすい。特に、孔面積が0.1 μm^2 以下の孔が増えると隣接する膜同士で固着が生じ、膜間へのポッティング剤の浸透不良によって中空糸膜内外の分離が不完全になる。このような固着による成型不良を無くすには、孔面積が0.1 μm^2 以下の孔の存在率を75%以下におさえる必要がある。より好ましくは60%以下、もっとも好ましくは45%以下である。

【0013】第二に平均孔面積について説明するが、本発明でいう平均孔面積とは、取り込んだ画像中の全ての孔の孔面積の平均値と定義され、下記の式(4)で与えられる。ここでも、10ピクセル以下はノイズと見なして計数から除外した。

$$\text{平均孔面積} = \text{画像中の孔面積の総和} / \text{画像中の孔総数} \quad (4)$$

★【0014】一方、これらのパラメーターに加えて外表面の開孔率も成型上、重要なパラメーターである。本発明でいう開孔率とは、取り込んだ画像の面積に対する開孔部の孔面積の総和の百分率と定義され、下記の式(5)で与えられる。ここでも、10ピクセル以下はノイズとみなして計数から除外した。

$$\text{開孔率 (\%)} = (\text{開孔部の孔面積の総和} / \text{取り込んだ画像の面積}) \times 100 \quad (5)$$

と、今度は膜の長軸方向へのしりや、すなわち、腰の強さが損なわれる結果、成型時にポッティング部での糸流れによる成型不良が多発する。腰の強さを損なわないために開孔率は30%を上限とすべきで、したがって、外表面の開孔率の範囲は10~30%であることが

必要である。より好ましい範囲は15〜30%である。

【0016】次に、本発明のポリスルホン系多孔質膜を製造する方法として、親水性高分子にポリビニルピロリドン（以下、PVPという）を用いる場合について例示する。該膜を製造するために用いる製膜原液は、ポリスルホン系樹脂、PVP、および溶媒の3成分を基本構成成分とする。製膜原液の組成として、ポリスルホン系樹脂の濃度は製膜可能な粘度を有し、かつ、膜としての特徴を発揮できる範囲であればよく、通常10〜25重量%、好ましくは15〜20重量%である。10重量%未満では膜としての十分な強度を得ることができず、25重量%を超えるとポリマー密度が高まって微通孔が減少し、十分な透過性能が得られないため実用的ではない。これらのポリスルホン系樹脂は、重量平均分子量が1〜5万のものが市販されており、それを使用すれば十分である。特に、限定はしない。

【0017】PVPは主としてポリスルホン系多孔質膜の孔形成、および残存して親水性を付与させるために使用される。驚くべきことに、PVPとポリスルホン系樹脂の割合が孔形成、特に膜の外表面における孔形成に関与していることが、本発明者らの鋭意研究の結果、見出された。詳細な原理は未だ不明な部分もあるが、ポリスルホン系樹脂に対してPVPの分子サイズがはるかに大きいことが主な要因ではないかと思われる。すなわち、ポリスルホン系樹脂に対するPVPの割合がある範囲で低くなると、吐出された原液粘度が低下してPVPの拡散によるミクロ相分離速度が早まって、PVPの小胞同志の融合が進む。その結果、数としては少ないが、比較的面積の大きい孔が形成される。反対にPVPの割合が高くなると、原液粘度の上昇のためにPVPの小胞同志の融合速度が低下し、その一方でポリスルホン系樹脂の析出が進行する結果として、面積の小さい孔が多数形成されて開孔率も高くなるものと考えられる。

【0018】このように膜の外表面に面積の大きい孔がある場合、たとえその数が少なくても、透析液中の菌塊片が孔から膜内部に侵入し、侵入時の物理的ショックで遊離したエンドトキシンが緻密層を通過して血液側に移行する可能性が生じてくる。反対に面積の小さい孔が増えると膜同志の固着が増えたり、開孔率が上がりすぎて膜の腰の強さが低下して、成型不良の要因となってくる。したがって、以上を満たすには、製膜原液におけるPVPのポリスルホン系樹脂に対する割合が0.25〜0.45が好ましく、0.30〜0.40であればさらに好ましい。

【0019】PVPは分子量別に様々な種類が市販されているので、それらを使用すればよく、特に限定はしない。ただし、上述のように外表面の開孔に重要であると同時に、膜表面を親水化する目的もある。この観点から、製膜時に膜表面に残存しやすいものが好ましく、分子量が大きいほどその傾向にあるので、重量平均分子

が少なくとも10万以上のものを使用するとよい。溶媒はポリスルホン系樹脂、およびPVPを共に溶解する溶媒であり、ジメチルスルホキシド、N、N-ジメチルアセトアミド、N、N-ジメチルホルムアミド、N-メチル-2-ピロリドン、スルホラン、ジオキサン等から選択されるが、これらの各々の組み合わせは任意である。また、凝固速度を制御する目的で少量の水や塩類を添加することもできる。

【0020】以上の系からなる製膜原液を用いてポリスルホン系多孔質膜を得るには、公知の乾湿式法を用いればよい。製膜原液と内部凝固液とを30〜60℃に保温された2重管構造の環状ノズル（二重紡糸口金）より同時に吐出し、凝固浴に導入する。その際、ノズル吐出から凝固浴に導入する前に空中走行させる。このノズルの吐出面と凝固浴表面の空中走行長は、通常10〜100cm、特に30〜85cmが好ましい。10cmより短いと凝固が不完全なまま凝固浴に達する結果、外表面にも緻密層が形成されるので本発明の膜が得られない。反対に100cmを超えると糸揺れが生じて凝固不完全な糸同志の接着が起こる可能性があり、製造プロセス上好ましくない。

【0021】また、空中走行部の雰囲気も、本発明を達成する上で重要であり、走行部周辺をフードで囲って密閉し、内部を湿潤状態に保持する。湿潤状態は下部の凝固浴から発生する水蒸気を利用し、凝固浴の温度を30〜70℃の範囲で調整して、フード内を水蒸気で飽和せればよい。より好ましくは45〜60℃の範囲である。内部凝固液は製膜原液に対して凝固性の高いものより、低いものを用いた方が糸糸安定性は良く、水と溶剤の混合液を用いることが好ましい。溶剤としてN、N-ジメチルアセトアミド、N、N-ジメチルホルムアミド、N-メチル-2-ピロリドン、ジメチルスルホキシド等から選択される。内部凝固液の好ましい組成は、溶剤が5〜40重量%であり、残りが水である。水の割合がこれ以上高まると、膜として十分な透水性が達成できない可能性がある。より好ましくは溶剤が10〜25重量%である。

【0022】上記のように凝固させた中空糸は、内表面側に緻密層、外表面に開孔部を有する非対称の多孔質構造を有している。この中空糸膜をカセに巻き取って一定束長にカットした後、残存している溶剤を水洗し、次いで、乾燥処理前に孔径保持剤として、例えば、グリセリン水溶液を付着させ、70〜80℃で10時間以上乾燥処理を行えば、本発明の膜が得られる。当該膜を使用する際には、両端をポリウレタン等でポッティングして所定の膜面積を有するモジュールに成型し、必要に応じて滅菌処理を行う。モジュール化は公知の方法に従えばよく、特に限定はしない。滅菌方法も用途に応じて公知の方法から選択すればよく、例えばエチレンオキシサイトガス滅菌、高圧蒸気滅菌、放射線滅菌等の処理をすればよ

い。

【0023】

【発明の実施の形態】次に、実施例および参考例によって本発明を詳細に説明するが、本発明は、それに限定されるものではない。なお、実施例で用いた諸数値は、以下の手順によって測定した。(外表面の孔面積、孔の存在率、および開孔率)膜を流水下で1時間水洗後、ドライアイス含有エタノールで凍結乾燥させた。この膜を専用の試料台に固定して銀蒸着後、走査型電子顕微鏡(日立製:S-2460N、以下、SEMという)にて倍率6000倍の外表面写真を撮影した。画像処理は、この写真(90mm×70mm)をイメージスキャナーで取り込み、処理ソフト(コージン・グラフィック・システムズ社製:カラマジション7、バージョン1.0)を用いて、取り込み範囲を写真全面、解像度320、明るさ2、256階調で実施した。この画像を処理ソフト(NIHイメージ、バージョン1.57)により二値化し、各々の孔の孔面積を算出した。なお、10ピクセル以下の画像はノイズと見なし、計数から除外した。また、電*

$$\text{逆濾過率 (\%)} = (C1/C0) \times 100$$

【0025】

【実施例1】ポリスルホン系樹脂(Amoco社製:P-1700)17重量%、PVP(BASF社製:K90)7重量%、N、N-ジメチルアセトアミド(以下、DMACという)76重量%を50℃で8時間攪拌溶解、脱泡し製膜原液を得た。内部凝固液はDMAC15重量%と水85重量%とを混和して調製した。この製膜原液と内部凝固液を55度に保温した二重紡糸口金から吐出させ、フードで密閉した60cmの空中走行部を経て凝固浴に導入した。凝固浴は52.5℃の温水とし、フード内部は水蒸気の飽和状態にあった。凝固浴を通過させ、カセに巻き取った膜を熱水で洗浄した。さらに孔径保持剤として15重量%のグリセリン水溶液を付着させ、70℃で12時間乾燥処理を行った。得られた膜を膜面積1.5m²のモジュールにポリウレタンを用いて成型し、水を充填して25KGyのγ線を照射した。この膜を図1に示すSEM写真をもとに画像処理した結果、外表面における孔面積0.5μm²以上の孔の割合が3.0%、孔面積0.1μm²以下の孔の割合が42.9%で、平均孔面積は0.16μm²、開孔率は15.5%であった。この膜は固着がなく、成形性は良好であった。また、逆濾過液中のエンドトキシン濃度は検出限界以下(9.0EU/リットル以下)であったため、事実上侵入を認めなかった。

【0026】

【実施例2】ポリスルホン系樹脂(Amoco社製:P-1700)17重量%、PVP(BASF社製:K90)4.5重量%、DMAC78.5重量%を混合し、50℃で8時間攪拌溶解、脱泡し製膜原液を得た。内部凝固液はDMAC20重量%と水80重量%とを混和し

*子線照射により孔径の揃ったメンブレンフィルター(ミリポア社製:アインポア、孔直径2μm)における真円の孔を同時測定して、キャリブレーションを行った。

【0024】(菌塊逆濾過試験)自家作成した高菌塊含有水溶液を用いて、透析液(AK-ソリタ・DL、清水製薬株式会社製)を調製した。用いた菌塊量は、エンドトキシンの含有量を測定することで代用した。エンドトキシン濃度として15800EU/リットルの菌塊汚染透析液を含む回路をモジュール透析液入側に接続し、透析液出側には栓をした。モジュールの血液出側に回路を接続、血液入側には栓をした。透析液入側回路にポンプをセットし、流速200cc/分にて2リットルを血液出側に逆濾過させて排出後、血液出側より逆濾過液を採取した。採取した逆濾過液中に含まれるエンドトキシン量をエンドスペシー(生化学工業社製:ES-50セット)により定量し、下記の式(6)から逆濾過率を算出した。なお、式中のC0は透析液中のエンドトキシン濃度、C1は逆濾過液中のエンドトキシン濃度を示す。

$$(6)$$

て調製した。空中走行長を45cm、凝固浴温度を65℃とした以外は、実施例1と同条件で乾燥膜を得た。得られた膜を膜面積1.5m²のモジュールにポリウレタンを用いて成型し、水を充填して25KGyのγ線を照射した。実施例1と同様に、SEM写真をもとに画像処理した結果、外表面における孔面積0.5μm²以上の孔の割合が9.3%、孔面積0.1μm²以下の孔の割合が39.6%で、平均孔面積が0.19μm²、開孔率が10.6%であった。この膜も固着はなく、良好に成型できた。また、逆濾過液中のエンドトキシン濃度は検出限界以下(9.0EU/リットル以下)であったため、事実上侵入を認めなかった。

【0027】

【比較例1】ポリスルホン系樹脂(Amoco社製:P-1700)17重量%、PVP(BASF社製:K90)9.0重量%、DMAC74.0重量%を混合し、50℃で8時間攪拌溶解、脱泡し製膜原液を得た。内部凝固液はDMAC20重量%と水80重量%とを混和して調製した。空中走行長を60cm、凝固浴温度を55℃とした以外は、実施例1と同条件で乾燥膜を得た。得られた膜を膜面積1.5m²のモジュールにポリウレタンを用いて成型し、水を充填して25KGyのγ線を照射した。この膜は、外表面における孔面積0.5μm²以上の孔の割合が0.8%、孔面積0.1μm²以下の孔の割合が8.5%であり、平均孔面積は0.03μm²、開孔率は3.3%であった。乾燥後は膜固着が激しく、そのままでは成型することができなかった。補修して成型後、菌塊逆濾過試験を実施したところ、逆濾過液中のエンドトキシン濃度は検出限界以下(9.0EU/リットル以下)と、事実上侵入を認めなかった。

【0028】

【比較例 2】ポリスルホン系樹脂（Amoco 社製：P-1700）17重量%、PVP（BASF 社製：K90）3.5重量%、DMAC 79.5重量%を混合し、50℃で8時間攪拌溶解、脱泡し製膜原液を得た。内部凝固液はDMAC 15重量%と水 85重量%とを混和して調製した。空中走行長を45cm、凝固浴温度を25℃とした以外は、実施例1と同条件で乾燥膜を得た。得られた膜を膜面積1.5m²のモジュールにポリウレタンを用いて成型し、水を充填して25KGyのγ線を照射した。この膜は、外表面における孔面積が0.5μm²以上の孔の割合が47.5%、孔面積が0.1μm²以下の孔の割合が18.8%で、平均孔面積は0.59μm²、開孔率は35.8%であった。乾燥後の膜固着*

*はなく、成型はできたが、ポッティング部全体に渡って糸流れが見られた。菌塊逆濾過試験を実施したところ、逆濾過率は0.13%であり、菌塊片の侵入によるエンドトキシンの逆濾過が認められた。

【0029】

【発明の効果】本発明のポリスルホン系多孔質膜は、製造時に膜固着による成型不良を起こすことなく、しかも、透析液に含まれる菌塊片が膜内部へ侵入してエンドトキシンの逆濾過が事実上起こらないため、血液浄化分野で好適に使用できる。

【図面の簡単な説明】

【図1】本発明で得られる膜の一例として、実施例1で得られた膜のSEM写真（倍率6000倍）を示す。

【図1】

図面代用写真



フロントページの続き

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(71)Applicant : ASAHI MEDICAL CO LTD

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(54) POROUS POLYSULFONE FILM

(57)Abstract:

PROBLEM TO BE SOLVED: To prevent bacterial lump pieces contained in a dialysis liquid from penetrating into the inside of a hollow fiber film which consists of a polysulfone resin and a hydrophilic polymer and has a dense layer at the inner surface side and a porous part on the outer surface by setting the ratio of pores each having a specified pore area, the average pore area, and the ratio of opening, each in a specified ratio.

SOLUTION: In a hollow fiber film which is suitably used for blood dialysis, blood filtration, and blood dialysis filtration, consists of a polysulfone resin and a hydrophilic polymer, and has a dense layer at the inner surface side and a porous part on the outer surface, the ratio of opening of the porous part on the outer surface is set at 10-30%; the ratio of pores each having a pore area of 0.5 μm^2 or higher, at 10% or lower; the ratio of pores each having a pore area of 0.1 μm^2 or lower, at 75% or lower; and/or the average pore area on the outer surface, in a range of 0.05-0.35 μm^2 . Thus, hollow fibers are prevented from adhering to each other, and simultaneously the penetration of bacterial lump pieces from a contaminated dialysis liquid into the inside of the film can be inhibited. Polyvinylpyrrolidone is preferable as the hydrophilic polymer.

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CLAIMS

[Claim(s)]

[Claim 1] It is the hollow fiber which consists of polysulfone system resin and a hydrophilic macromolecule, has a compact layer in an internal-surface side, and has an aperture in an outside surface. a hole [in / in the hole density of the aperture in an outside surface / 10 - 30%, and an outside surface] -- area -- 0.5micrometer² the abundance of the above hole -- 10% or less and a hole -- area -- 0.1micrometer² the abundance of the following holes is 75% or less -- and/or, the average hole area in an outside surface -- 0.05-0.35micrometer² it is -- polysulfone system porous membrane characterized by things.

[Claim 2] Polysulfone system porous membrane according to claim 1 characterized by a hydrophilic giant molecule being a polyvinyl pyrrolidone.

[Translation done.]

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention is used about the medical-application demarcation membrane aiming at removal of the wastes in blood by extracorporeal circulation in the hemodialysis for substituting for blood purification, especially a kidney function, hemofiltration, and the field of hemofiltration dialysis.

[0002]

[Description of the Prior Art] In recent years, dialysis using permeable membrane is performed by the fall of a kidney function to a patient with the low wastes removal capacity in blood, a patient's prolongation of life is made, and it is. On the other hand, the complication called dialysis amyloidosis has appeared with protraction of such dialysis. This is a disease which the fiber protein called amyloid carries out deposition to a ligament, a tendon, a joint, etc., and brings about various clinical manifestations. Since beta 2-microglobulin was identified as one of the proteins which constitute this amyloid, removal of these low-molecular protein is one of the therapy targets, and the commercial-scene demand of the high performance permeable membrane which makes it possible has increased. Although it is the high removal engine performance and the outstanding biocompatibility of the low-molecular protein represented by beta2-microglobulin as a property for which high performance permeable membrane is asked, the polysulfone system resin which is synthetic macromolecule as a film material with which are satisfied of these attracts attention, and development of the high performance permeable membrane which makes polysulfone system resin a subject is furthered positively.

[0003] However, if polysulfone system resin has high hydrophobicity and it remains as it is, since water wettability is bad, a filtration efficiency cannot fully demonstrate it. Furthermore, when used in the blood purification field like this invention, it is necessary to control activation of a blood coagulation system, and in order to carry out hydrophilization of the film front face, hydrophilization agents, such as a hydrophilic macromolecule and a glycerol, are added in many cases. Since these hydrophilization agents exist in a film front face, as a result of fixing arising by the film by which a hydrophilization agent achieves the duty of a paste and adjoins at the time of the desiccation in a manufacture process, poor molding by poor osmosis of a potting agent might occur.

[0004] The attempt which improves this fault is indicated by JP.7-289863,A as a technique which mitigates the touch area of the film which make a big aperture to the outside surface of a hollow fiber, and adjoin it. however -- while the water quality management situation of dialysing fluid improved by leaps and bounds by use of an endotoxin cut-off filter -- ****, such as a dialysing fluid supply coupler, -- the dialysing fluid contamination incidentally depended was still generated, and the piece of a sulfur granule which peeled and fell from the coupler at the time of use may have invaded into the porosity section inside the film from the aperture of a film outside surface. And in these high performance permeable membrane, there was a possibility of the endotoxin isolated from the piece of a sulfur granule with the physical shock at the time of invasion having penetrated a compact layer, having shifted to a blood side, and stimulating a living body.

[0005]

[Problem(s) to be Solved by the Invention] Moreover, this invention aims at offering the polysulfone

system porous membrane by which the piece of a sulfur granule contained in dialysing fluid does not trespass upon the interior of the film, without causing poor molding by film fixing at the time of manufacture.

[0006]

[Means for Solving the Problem] In the hollow fiber which consisted of polysulfone system resin and a hydrophilic macromolecule, had a compact layer in the internal-surface side, and had an aperture in the outside surface as a result of inquiring wholeheartedly, in order that this invention persons may solve the above-mentioned technical problem When abundance of a specific hole area, average hole area, and hole density were made into the specific range, it resulted it not only can prevent fixing of hollow filaments, but that it could prevent invasion to the interior of the film of the piece of a sulfur granule originating in contamination dialysing fluid to high rate in the header, and this invention was resulted in *****. Namely, this invention consists of polysulfone system resin and a hydrophilic macromolecule, a hole [in / in the hole density of the aperture / in / it is a hollow fiber and / an outside surface / which has a compact layer in an internal-surface side, and has an aperture in an outside surface / 10 - 30%, and an outside surface] -- area -- 0.5micrometer² The abundance of the above hole at 10% or less and a hole -- area -- 0.1micrometer² the average hole area in that the abundance of the following holes is 75% or less, and/or an outside surface -- 0.05-0.35micrometer² it is -- it is related with the polysulfone system porous membrane characterized by things.

[0007] Although the film of this invention consists of polysulfone system resin and a hydrophilic macromolecule, the main components which constitute the film are polysulfone system resin, and consist of a chemical structure type (1) shown below or repeat structure of the unit of (2). The so-called polysulfone derivative which the functional group and the alkyl group combined on the ring besides this is also contained under the category of this invention. In addition, Ar in a formula shows the bivalence phenyl group of the Para permutation.

-O-Ar-C(CH₃)₃-Ar-O-Ar-SO₃-Ar- (1)

-O-Ar-SO₃-Ar- (2)

[0008] The second component which constitutes the film is a hydrophilic macromolecule, and is mainly added for the purpose of membranous hydrophilization and hole formation. A hydrophilic giant molecule dissolves in polysulfone system resin and a common solvent, and the point of having compatibility to a vinyl system giant molecule is desirable, for example, can choose it from a polyvinyl pyrrolidone, a polyethylene glycol, a polyamide, polyvinyl alcohol, and an ethylene-vinylalcohol copolymer. Especially, since a polyvinyl pyrrolidone has polysulfone system resin and moderate compatibility, remains in a film front face and can be contributed to the formation of an anti-thrombus and filtration efficiency by hydrophilization, it is the most desirable. Since what is necessary is have just carried out the hydrophilization of the film front face finally about the content of these hydrophilic macromolecules, it is enough if it is 3 - 12 % of the weight. It is 5 - 9 % of the weight more preferably. Therefore, the membranous remaining part and 88 - 97 % of the weight are polysulfone system resin.

[0009] The structure of the porous membrane of this invention has the shape of a hollow filament with the centrum whose bore is 80-400 micrometers, and the thickness section whose thickness is 35-85 micrometers, and has pressure resistance and tensile strength sufficient as a blood purification application. If a bore is less than [this] small, vascular resistance increases and a flow velocity cannot be secured, but even if it becomes large beyond the need, the mass transfer effectiveness in blood falls and it leads to the fall of a curative effect. Moreover, if thickness is too thin, it will cause crushing and leak, without the ability maintaining reinforcement, if too thick, the mass transfer resistance in the film will become large, and penetrable ability will fall. the hole moreover controlled by nothing and the outside surface which touches dialysing fluid in the unsymmetrical structure where this hollow fiber is from the layer of condensation and rarefaction as a base material on a compact layer [which has isolation in an internal-surface side], and outside-surface side -- it has an aperture with distribution and the effectiveness of this invention is demonstrated.

[0010] Hole distribution of the film of this invention is evaluated by carrying out image analysis of the scanning electron microscope photograph of the outside surface of the desiccation film. The silver vacuum evaporation of the film freeze-dried from cold ethanol is carried out after rinsing the aperture maintenance material and sealing liquid which specifically adhered to the film, and the outside-surface photograph of the film in one 6000 times the scale factor of this is taken with an

electron microscope, printing this on 90mmx70mm magnitude, downloading all the range of a photograph to a personal computer using image-analysis software, and carrying out binarization of the image -- each aperture of an outside surface -- a hole -- it can ask for area. consequently, this invention persons -- a hole -- it found out that fixed relation also between that fixed relation between distribution of area, average hole area, and the amount of piece invasion of a sulfur granule in dialysing fluid and moldability is and hole density, and a moldability was, and there was the need of controlling all.

[0011] Although the abundance of a hole which has a specific hole area is explained in the first place first, with the abundance as used in the field of this invention, it is defined as the percentage of the total of the hole of the hole area of the arbitration to the total of the hole in the captured image, and is given by the following formula (3). In addition, it was regarded as the noise and 10 pixels or less were excepted from counting.

Abundance (%) = (total of hole in total/image of hole of hole area of arbitration) x100 (3)

[0012] Usually, although some dialysing fluid flows into the porous section inside the film from the aperture of a membranous outside surface, if the piece of a sulfur granule of the origins, such as a coupler, is contained in the dialysing fluid, the piece of a sulfur granule will invade to the interior of the film, a part of physical endotoxin at the time of invasion shocking and isolated from the piece of a sulfur granule may pass a compact layer, and it may shift to a blood side. Generally, for the magnitude of a fungus body, since a major axis is 1-3 micrometers, hole area is 2 0.5 micrometers. Below, invasion of the piece of a sulfur granule hardly takes place. In order to prevent invasion of the piece of a sulfur granule as a matter of fact, it is hole area 0.5micrometer². It is required to stop the abundance of the above hole to 10% or less, and it is still more desirable when it stops to 7% or less. But it is 5% or less preferably. If holes with small one side and hole area increase in number too much, the problem on molding will tend to arise shortly. especially -- a hole -- area -- 0.1micrometer² Fixing arises by the film which adjoin if the following holes increase in number, and separation of hollow fiber inside and outside becomes imperfect by poor osmosis of the potting agent of a between [film]. for losing poor molding by such fixing -- a hole -- area -- 0.1micrometer² It is necessary to press down the abundance of the following holes to 75% or less. It is 45% or less most preferably 60% or less.

[0013] Although average hole area is explained to the second, with the average hole area as used in the field of this invention, it is defined as the average of the hole area of all the holes in the captured image, and is given by the following formula (4). Here, it was regarded as the noise and 10 pixels or less were excepted from counting.

Average hole area = hole total in total/image of the hole area in an image (4)

Average hole area is also related not only to invasion of the piece of a sulfur granule but fixing of moldability, especially film. The inclination which the film which adjoin, so that it is small fixes becomes strong, and this tends to produce poor molding. Since invasion of the piece of a sulfur granule takes place so that it is large on the contrary, it is 2 0.05-0.35 micrometers. It is necessary to hold down to the range. more -- desirable -- 0.10-0.30micrometer² -- most -- desirable -- 0.10-0.20micrometer² It is the range.

[0014] On the other hand, in addition to these parameters, the hole density of an outside surface is also an important parameter on shaping. With the hole density as used in the field of this invention, it is defined as the percentage of total of the hole area of the aperture to the area of the captured image, and is given by the following formula (5). Here, it was regarded as the noise and 10 pixels or less were excepted from counting.

Hole density (%) = (total [of the hole area of an aperture] / area of captured image) x100 (5)

[0015] Hole density participates in the contribution to fixing of film greatly, its touch area of the film which adjoin if hole density is small increases, fixing takes place, and when severe, the whole bundle may fix in the shape of a rod. For this reason, hole density needs to secure 10% or more. However, shortly, if hole density is enlarged superfluously, as a result of [to the membranous direction of a major axis] coming to carry out, namely, spoiling nerve, poor molding by the yarn flow in the potting section will occur frequently at the time of molding. In order not to spoil nerve, hole density should make 30% an upper limit, therefore the range of the hole density of an outside surface needs to be 10 - 30%. The more desirable range is 15 - 30%.

[0016] Next, it illustrates as an approach of manufacturing the polysulfone system porous membrane

of this invention, about the case where a polyvinyl pyrrolidone (henceforth PVP) is used for a hydrophilic giant molecule. The film production undiluted solution used in order to manufacture this film makes a basic constituent polysulfone system resin, PVP, and three components of a solvent. As a presentation of a film production undiluted solution, the concentration of polysulfone system resin is usually 15 - 20 % of the weight preferably ten to 25% of the weight that what is necessary is just the range which has the viscosity which can produce a film and can demonstrate the description as film. At less than 10 % of the weight, since a polymer consistency will increase, a practice through-hole will decrease and sufficient penetrable ability will not be obtained if sufficient reinforcement as film cannot be obtained but it exceeds 25 % of the weight, it is not practical. These polysulfone system resin is enough, if the thing of 10,000-50,000 is marketed and weight average molecular weight uses it. Especially limitation is not carried out.

[0017] PVP is used in order to hole-form, and for polysulfone system porous membrane to mainly remain and to make a hydrophilic property give. a hole [in / to a surprising thing / in the rate of PVP and polysulfone system resin / the outside surface of hole formation, especially the film] — participating in formation was found out as a result of wholeheartedly research of this invention persons. Although a detailed principle also has a still unknown part, it is thought to polysulfone system resin that it is the main factors that the molecule size of PVP is far large. That is, if it becomes low in the range with the rate of PVP to polysulfone system resin, the breathed-out undiluted solution viscosity will fall, the microfacies separation rate by diffusion of PVP will be rash, and fusion of the vesicle comrade of PVP will progress. Consequently, although it is few as a number, a hole with a comparatively large area is formed. If the rate of PVP becomes high on the contrary, the fusion rate of the vesicle comrade of PVP will fall for the rise of undiluted solution viscosity, and it will be thought that many holes with an area small as a result with which a deposit of polysulfone system resin advances on the other hand are formed, and hole density also becomes high.

[0018] Thus, when a hole with a large area is shown in a membranous outside surface, possibility that the endotoxin which the piece of a sulfur granule in dialysing fluid trespassed [the number] upon the interior of the film from the hole at least, and separated with the physical shock at the time of invasion will pass a compact layer, and will shift to a blood side even if arises. If holes with an area small on the contrary increase in number, fixing of film will increase, or hole density increases too much, membranous nerve falls, and it becomes the factor of poor molding. Therefore, in order to fill the above, 0.25-0.45 have a desirable rate to the polysulfone system resin of PVP in a film production undiluted solution, and it is still more desirable if it is 0.30-0.40.

[0019] Especially limitation is not carried out that PVP should just use them since various classes are marketed according to molecular weight. However, while it is important for puncturing of an outside surface as mentioned above, there is also the purpose which carries out hydrophilization of the film front face. Since it is in that inclination from this viewpoint so that what is easy to remain on a film front face at the time of film production is desirable and molecular weight is large, it is good for weight average molecular weight to use at least 100,000 or more things. Although both solvents are solvents which dissolve polysulfone system resin and PVP and are chosen from dimethyl sulfo KISHINDO, N,N-dimethylacetamide, N,N-dimethylformamide, a N-methyl-2-pyrrolidone, a sulfone, dioxane, etc., such combination is arbitrary in each. Moreover, little water and salts can also be added in order to control a coagulation rate.

[0020] What is necessary is just to use a well-known dryness-and-moisture type method, in order to obtain polysulfone system porous membrane using the film production undiluted solution which consists of the above system. A film production undiluted solution and internal coagulation liquid are introduced into coincidence at discharge and a coagulation bath from the annular nozzle (duplex spinneret) of the double tubing structure kept warm by 30-60 degrees C. In that case, air transit is carried out, before introducing into a coagulation bath from the nozzle regurgitation. Especially the air transit length on the regurgitation side of this nozzle and the front face of a coagulation bath usually has 30-85 desirablecm 10-100cm. As a result of reaching a coagulation bath while coagulation has been imperfect if shorter than 10cm, since a compact layer is formed also in an outside surface, the film of this invention is not obtained. if it exceeds 100cm on the contrary — a yarn shake — being generated — coagulation — adhesion of imperfect yarn may take place and it is not desirable on a manufacture process.

[0021] Moreover, the ambient atmosphere of the air transit section is also important when attaining this invention, the transit section circumference is enclosed and sealed with a hood, and the interior is held to a damp or wet condition. A damp or wet condition uses the steam generated from a lower coagulation bath, adjusts the temperature of a coagulation bath in 30-70 degrees C, and should just saturate the inside of a hood with a steam. It is the range of 45-60 degrees C more preferably. As for internal coagulation liquid, it is desirable for spinning stability to be [it] better to use a thing lower than the high thing of freezing characteristic to a film production undiluted solution, and to use the mixed liquor of water and a solvent. It is chosen from N,N-dimethylacetamide, N,N-dimethylformamide, a N-methyl-2-pyrrolidone, dimethyl sulfoxide, etc. as a solvent. A solvent is 5 - 40 % of the weight, and the remainder of the desirable presentation of internal coagulation liquid is water. If the rate of water increases more than this, permeable ability sufficient as film may be unable to attain. A solvent is 10 - 25 % of the weight more preferably.

[0022] The hollow filament made to solidify as mentioned above has the unsymmetrical vesicular structure to which it has a compact layer in an internal-surface side, and it has an aperture in an outside surface. After rolling round this hollow fiber to skein and cutting into fixed bundle length, an extant solvent is rinsed, and if for example, a glycerol water solution is made to adhere and desiccation processing is performed at 70-80 degrees C for 10 hours or more, subsequently to before desiccation processing, the film of this invention will be obtained as an aperture hold-back agent. In case the film concerned is used, it casts to the module which carries out potting of the both ends with polyurethane etc., and has a predetermined film surface product, and sterilization processing is performed if needed. Especially limitation is not carried out that a modularization should just follow a well-known approach. What is necessary is just to process ethylene OKISAITOGASU sterilization, autoclave sterilization, radappertization, etc. that what is necessary is just to also choose the sterilization approach from a well-known approach according to an application.

[0023]

[Embodiment of the Invention] Next, although an example and the example of reference explain this invention to a detail, this invention is not limited to it. In addition, many numeric values used in the example were measured with the following procedures. (The hole area of an outside surface, abundance of a hole, and hole density) the film -- a stream -- it was made to freeze-dry by dry ice content ethanol after 1-hour rinsing in the bottom It fixed to the sample base of dedication of this film, and the outside-surface photograph 6000 times the scale factor of this was taken after silver vacuum evaporation with the scanning electron microscope (made in Hitachi: call it SEM S-2460 Ns and the following). The image processing incorporated this photograph (90mmx70mm) with the image scanner, and carried out the incorporation range with whole photograph surface, resolution 320, and brightness 2,256 gradation using processing software (the product made from KOSHIN GURAFIKU cis- TAMUZU: the color magician 7, version 1.0). Binarization of this image was carried out with processing software (a NIH image, version 1.57), and the hole area of each hole was computed. In addition, it considered that an image 10 pixels or less was a noise, and it was excepted from counting. Moreover, the hole of the perfect circle in the membrane filter (Millipore [Corp.] make: eye SOPOA, hole diameter of 2 micrometers) to which the aperture was equal with electron beam irradiation was measured simultaneously, and carry BURISHON was performed.

[0024] (Sulfur granule reverse filtration trial) Dialysing fluid (AK-Solita and DL, the Shimizu Pharmaceuticals incorporated company make) was prepared using the high sulfur granule content water solution which carried out private creation. It substituted measuring the content of endotoxin for the used amount of sulfur granules. The circuit which contains the sulfur granule contamination dialysing fluid of 15800EU / liter as endotoxin concentration was connected to the module dialysing fluid close side, and the plug was turned on the dialysing fluid appearance side. The plug was turned for the circuit on the modular blood appearance side at the connection and blood close side. Set the pump to the dialysing fluid close side circuit, 2l. was made to reverse-part [for 200 cc/of the rates of flow] filter to a blood appearance side, and reverse filtrate was extracted after discharge and from a blood appearance side. The quantum of the amount of endotoxins contained in the extracted reverse filtrate was carried out by end SUPESHI - (Seikagaku make: ES-50 set), and the reverse filtration fraction was computed from the following formula (6). In addition, C0 in a formula shows the endotoxin concentration in dialysing fluid, and C1 shows the endotoxin concentration in reverse filtrate.

Reverse filtration-fraction (%) = $(C1/C0) \times 100$ (6)

[0025]

[Example 1] At 50 degrees C, it stirring-dissolved, degassing of 17 % of the weight (the product made from Amoco-- 1700) of polysulfone system resin, 7 % of the weight (BASF [A.G.] make: K90) of PVP, and the 76 % of the weight (henceforth DMAC) of the N,N-dimethylacetamide was carried out for 8 hours, and the film production undiluted solution was obtained. It mixed with internal coagulation liquid and it prepared 15 % of the weight of DMAC, and 85 % of the weight of water. It was made to breathe out from the duplex spinneret which kept warm this film production undiluted solution and internal coagulation liquid at 55 degrees, and introduced into the coagulation bath through the 60cm air transit section sealed with the hood. The coagulation bath considered as 52.5-degree C warm water, and the interior of a hood suited the saturation state of a steam. The coagulation bath was passed and hot water washed the film rolled round to skein. 15% of the weight of the glycerol water solution was made to adhere as an aperture hold-back agent furthermore, and desiccation processing was performed at 70 degrees C for 12 hours. It is the obtained film 1.5m of film surface products 2 Polyurethane was used and cast to the module, it was filled up with water, and the gamma ray of 25KG(ies) was irradiated. Hole area 0.5micrometer² [in / as a result of carrying out an image processing based on the SEM photograph which shows this film to drawing 1 / an outside surface] The rate of the above hole is 3.0% and hole area 0.1micrometer². As for average hole area, at 42.9%, 0.16 micrometers of the percentages of the following holes of 2 and hole density were 15.5%. This film did not have fixing and the moldability was good. Moreover, since the endotoxin concentration in reverse filtrate was below limit of detection (below 9.0EU / liter), it did not accept invasion as a matter of fact.

[0026]

[Example 2] 17 % of the weight (the product made from Amoco-- 1700) of polysulfone system resin, 4.5 % of the weight (BASF [A.G.] make: K90) of PVP, and 78.5 % of the weight of DMAC were mixed, at 50 degrees C, it stirring-dissolved, degassing was carried out for 8 hours, and the film production undiluted solution was obtained. It mixed with internal coagulation liquid and it prepared 20 % of the weight of DMAC, and 80 % of the weight of water. The desiccation film was obtained on an example 1 and these conditions except having made air transit length to 45cm, and having made coagulation bath temperature into 65 degrees C. It is the obtained film 1.5m of film surface products 2 Polyurethane was used and cast to the module, it was filled up with water, and the gamma ray of 25KG(ies) was irradiated. Hole area 0.5micrometer² [in / as a result of carrying out an image processing based on a SEM photograph like an example 1 / an outside surface] The rate of the above hole is 9.3% and hole area 0.1micrometer². For the percentage of the following holes, at 39.6%, average hole area was [0.19 micrometers of 2 and hole density] 10.6%. This film does not exist, either and fixing has cast it good. Moreover, since the endotoxin concentration in reverse filtrate was below limit of detection (below 9.0EU / liter), it did not accept invasion as a matter of fact.

[0027]

[The example 1 of a comparison] 17 % of the weight (the product made from Amoco-- 1700) of polysulfone system resin, 9.0 % of the weight (BASF [A.G.] make: K90) of PVP, and 74.0 % of the weight of DMAC were mixed, at 50 degrees C, it stirring-dissolved, degassing was carried out for 8 hours, and the film production undiluted solution was obtained. It mixed with internal coagulation liquid and it prepared 20 % of the weight of DMAC, and 80 % of the weight of water. The desiccation film was obtained on an example 1 and these conditions except having made air transit length to 60cm, and having made coagulation bath temperature into 55 degrees C. It is the obtained film 1.5m of film surface products 2 Polyurethane was used and cast to the module, it was filled up with water, and the gamma ray of 25KG(ies) was irradiated. This film is hole area 0.5micrometer² in an outside surface. The rate of the above hole is 0.8% and hole area 0.1micrometer². The percentage of the following holes was 88.5% and 0.03 micrometers of 2 and hole density of average hole area were 3.3%. After desiccation was not able to be cast, if film fixing was intense and remained as it was. When it repaired and the sulfur granule reverse filtration trial was carried out after molding, the endotoxin concentration in reverse filtrate did not accept invasion as a matter of fact below limit of detection (below 9.0EU / liter).

[0028]

[The example 2 of a comparison] 17 % of the weight (the product made from Amoco-- 1700) of

polysulfone system resin, 3.5 % of the weight (BASF [A.G.] make: K90) of PVP, and 79.5 % of the weight of DMAC were mixed, at 50 degrees C, it stirring-dissolved, degassing was carried out for 8 hours, and the film production undiluted solution was obtained. It mixed with internal coagulation liquid and it prepared 15 % of the weight of DMAC, and 85 % of the weight of water. The desiccation film was obtained on an example 1 and these conditions except having made air transit length to 45cm, and having made coagulation bath temperature into 25 degrees C. It is the obtained film 1.5m of film surface products 2 Polyurethane was used and cast to the module, it was filled up with water, and the gamma ray of 25KG(ies) was irradiated. a hole [in / in this film / an outside surface] -- area -- 0.5micrometer² the rate of the above hole -- 47.5% and a hole -- area -- 0.1micrometer² The percentage of the following holes was 18.8% and 0.59 micrometers of 2 and hole density of average hole area were 35.8%. Although there is no film fixing after desiccation and molding was completed, yarn flow was seen over the whole potting section. When the sulfur granule reverse filtration trial was carried out, the reverse filtration fraction is 0.13% and reverse filtration of the endotoxin by invasion of the piece of a sulfur granule was accepted.

[0029]

[Effect of the Invention] Since the piece of a sulfur granule contained in dialysing fluid moreover trespasses upon the interior of the film and reverse filtration of endotoxin does not take place as a matter of fact, without causing poor molding by film fixing at the time of manufacture, the polysulfone system porous membrane of this invention can be suitably used in the blood purification field.

[Translation done.]

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DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]

[Drawing 1] As an example of the film obtained by this invention, the SEM photograph (one 6000 times the scale factor of this) of the film obtained in the example 1 is shown.

[Translation done.]

* NOTICES *

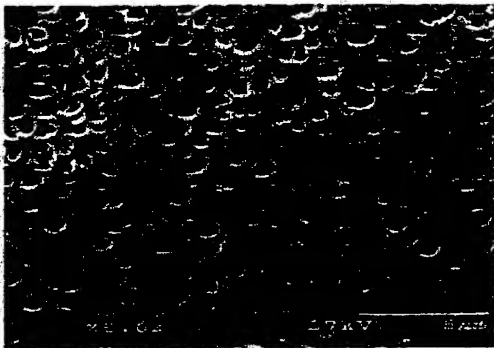
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DRAWINGS

[Drawing 1]

図面代用写真



[Translation done.]